Package leaflet: Information for the user
Paricalcitol 5 micrograms/mL solution for injection
paricalcitol

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Paricalcitol is and what it is used for
Paricalcitol is artificially made (synthetic analogue) activated vitamin D. It is used to prevent and treat high levels of parathyroid hormone in the blood in people who have kidney failure and are being treated on a kidney machine (haemodialysis). High levels of parathyroid hormone can be caused by low levels of "activated" vitamin D in patients with kidney failure.

Activated vitamin D is required for normal functioning of many tissues of the body, including the kidneys and bones.

2. What you need to know before you are given Paricalcitol
You should not be given Paricalcitol:
- if you are allergic to paricalcitol or any of the other ingredients of this medicine (listed in section 6).
- if you have very high levels of calcium or vitamin D in your blood. Your doctor will monitor your blood levels and be able to tell you if these conditions apply to you.

Warnings and precautions
- Before the treatment begins, it is important to limit the amount of phosphorus in your diet. Examples of foods high in phosphorous include tea, soda, beer, cheese, milk, cream, fish, chicken or beef liver, beans, peas, cereals, nuts and grains.
- Phosphate-binding medicines, which keep phosphate from being absorbed from your food, may be needed to control phosphorus levels.
- If you are taking calcium-based phosphate binders, the doctor may need to adjust your dose.
- Your doctor will need to do blood tests to monitor your treatment.

Other medicines and Paricalcitol
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines.

Some medicines can affect the action of Paricalcitol or make side effects more likely. It is particularly important to tell your doctor if you are taking any of the following medicines:
- to treat fungal infections such as candida or thrush (i.e. ketoconazole)
- to treat heart or blood pressure (e.g. digoxin and diuretics or water pills)
- that contain magnesium (e.g. some types of indigestion medicines called antacids, such as magnesium trisilicate)
- that contain aluminium (e.g. phosphate-binders, such as aluminium hydroxide)
- that contain phosphate or vitamin D which should not be taken concomitantly with paricalcitol
- that contain high doses of calcium

Ask your doctor, nurse or pharmacist for advice before taking any medicine.

Paricalcitol with food and drink
Paricalcitol may be given with or without food.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

It is not known if it is safe for pregnant or breast-feeding women to be given this medicine. Therefore, it should only be used after discussion with your doctor, who will help you make the best decision for you.

Driving and using machines
Whilst you are being treated with Paricalcitol, your ability to drive safely or use heavy machines may be affected. Paricalcitol may make you feel dizzy, weak and/or drowsy.

Do not drive or use machines if you feel these symptoms.

Paricalcitol contains ethanol (alcohol)
This medicine contains 20% v/v of ethanol (alcohol), i.e. up to 1.3 g per dose, equivalent to 33.2 mL beer, 13.8 mL wine per dose. Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease or epilepsy.

3. How Paricalcitol will be given
Your doctor will use the results of your laboratory tests to decide the correct starting dose for you. Once treatment with Paricalcitol has started, the dose may be adjusted, based upon the results of routine laboratory tests. Using your lab results, your doctor will help determine the correct dose of Paricalcitol for you.

Paricalcitol will be given by a doctor or nurse while you are having your treatment on the kidney machine. It will be given through the tube (bloodline) that is used to connect you to the machine. You will not need to have an injection because Paricalcitol can be put directly into the tube that is being used for your treatment. You will not be given Paricalcitol more frequently than every other day and not more than three times a week.

If you are given more Paricalcitol than you should
Too much Paricalcitol may lead to high levels of calcium (in the blood and urine) and phosphate in the blood that may require treatment. Additionally, too much Paricalcitol may reduce parathyroid hormone levels. Symptoms which can appear soon after receiving too much Paricalcitol include:
- feeling weak and/or drowsy
- headache
- feeling sick or being sick
- dry mouth, constipation
- pain in muscles or bones
- unusual taste in the mouth

Symptoms which can develop over a longer period of receiving too much Paricalcitol include:
- loss of appetite
- drowsiness
- weight loss
- sore eyes
- runny nose
- itchy skin
- feeling hot and feverish
- loss of sex drive
- severe abdominal pain
- kidney stones
- Your blood pressure may be affected and awareness of your own heartbeat (palpitations) can occur.

If you experience high levels of calcium in your blood after being given Paricalcitol, your doctor will ensure you receive the appropriate treatment to return your calcium to normal limits. Once your calcium levels return to normal limits, you may be given Paricalcitol at a lower dose.

However, your doctor will be checking your blood levels and **if you experience any of the above, seek medical advice immediately.**

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Various allergic reactions have been seen with paricalcitol. **Important: Tell your doctor or nurse immediately, if you notice any of the following side effects:**
- Shortness of breath
- Difficulty breathing or swallowing
- Wheezing
- A rash, itchy skin or hives
- Swelling of the face, lips, mouth, tongue or throat.

Tell your doctor or nurse, if you notice any of the following side effects:

Common: may affect up to 1 in 10 people
- headache
- unusual taste in the mouth
- itchy skin
- low levels of parathyroid hormone
- high levels of calcium (feeling sick or being sick, constipated or confused); phosphorous in the blood (probably no symptoms but it can make bones more likely to break)

Uncommon: may affect up to 1 in 100 people
- allergic reactions (such as shortness of breath, wheezing, rash, itching or swelling of the face and lips); itchy blisters
- blood infection; decreased number of red cells (anaemia – feeling weak, shortness of breath, looking pale); decreased number of white cells (more likely to get infections); swollen glands in the neck, armpit and/or groin; increased bleeding time (blood will not clot so quickly)
- heart attack; stroke; chest pain; irregular/fast heartbeat; low blood pressure; high blood pressure;
- coma (a deep state of unconsciousness during which the person cannot respond to the environment)
- unusual tiredness, weakness; dizziness; fainting
- injection site pain
- pneumonia (lung infection); fluid on the lungs; asthma (wheezing, cough, difficulty breathing);

- sore throat; cold; fever; flu-like symptoms; pink eye (itchy/crusty eyelids); increased pressure in the eye; earache; nose bleeds
- nervous twitches; confusion, which is sometimes severe (delirium); agitation (feeling jittery, anxious); nervousness; personality disorders (not feeling like yourself);
- tingling or numbness; decreased touch sensation; problems sleeping; sweating at night; muscular spasms in arms and legs, even during sleep;
- dry mouth; thirsty; nausea; difficulty swallowing; vomiting; loss of appetite; weight loss; heart burn; diarrhoea and stomach ache; constipation: bleeding from the rectum;
- difficulty having an erection; breast cancer; infections in the vagina
- breast pain; back pain; joint/muscular pain; feeling of heaviness caused by general swelling or localized swelling of the ankles, feet and legs (oedema); abnormal way of walking;
- hair loss; excessive hair growth,
- increase of a liver enzyme; high levels of parathyroid hormones; high levels of potassium in the blood; low levels of calcium in the blood

Not known: frequency cannot be estimated from the available data
- swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing; itchy skin (hives). Stomach bleeding. **If you notice these symptoms, get medical help immediately.**

You may not be able to tell if you have some of the side effects listed above unless you are told so by your doctor.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance Earlsfort Terrace IRL - Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517, Website: www.hpra.ie, e-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Paricalcitol
Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the ampoule after "EXP". The expiry date refers to the last day of that month.

Keep the ampoules in the outer carton in order to protect from light.

For single use only.

Paricalcitol should be used immediately after opening.

Do not use this medicine if you notice particles or discolouration.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information
What Paricalcitol contains
- The active substance is paricalcitol.
  Each mL of solution for injection contains 5 micrograms of paricalcitol.
  Each 1 mL ampoule contains 5 micrograms of paricalcitol.
  Each 2 mL ampoule contains 10 micrograms of paricalcitol.
- The other ingredients are: ethanol, macrogol 15 hydroxystearate and water for injection.

What Paricalcitol looks like and contents of the pack
Paricalcitol solution for injection is a watery, clear and colourless solution, free from visible particles.
It is supplied in containers with 5 glass ampoules type I of 1 mL or 2 mL.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
Pinewood Laboratories Ltd.,
Ballymacarbry,
Clonmel,
Co. Tipperary, Ireland

Manufacturer
Pharmathen
6, Dervenakion str.
153 51 Pallini Attiki; Greece

This medicinal product is authorised in the Member States of the EEA under the following names:
Denmark: Paricalcitol "Pharmathen" 2microgram/ml & 5microgram/ml
Greece: Panozin 2µg/ml & 5µg/ml
Portugal: Paricalcitol/Pharmathen 2µg/ml & 5µg/ml
Ireland: Paricalcitol 5 micrograms/mL solution for injection

This leaflet was last revised in 01/2020.

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The following information is intended for healthcare professionals only:

Paricalcitol 5 micrograms/mL solution for injection

Preparation of solution for injection
Paricalcitol 5 micrograms/mL solution for injection is intended for single use only. As with all medicines administered through injection, the diluted solution should be inspected for particles and discoloration, prior to administration.

Compatibility
This medicine must not be mixed with other medicines.

Storage and shelf life
Parenteral medicines should be inspected visually for particulate matter and discoloration prior to administration. The solution is clear and colourless.

Keep the ampoules in the outer carton in order to protect from light.
This medicine has a shelf life of 2 years.
Paricalcitol should be used immediately after opening.

Posology and Method of Administration
Paricalcitol solution for injection is administered via haemodialysis access.

Adults
1) Initial Dose should be calculated based on baseline parathyroid hormone (PTH) levels:

The initial dose of paricalcitol is based on the following formula:

$$\text{Initial dose (micrograms)} = \frac{\text{baseline intact PTH level in pmol/L}}{8}$$

OR

$$= \frac{\text{baseline intact PTH level in pg/mL}}{80}$$

and administered as an intravenous (IV) bolus dose no more frequently then every other day at any time during dialysis.

The maximum dose safely administered in clinical studies was as high as 40 micrograms.

2) Titration Dose:

The currently accepted target range for PTH levels in end-stage renal failure subjects undergoing dialysis is no more than 1.5 to 3 times the non-uremic upper limit of normal, 15.9 to 31.8 pmol/L (150-300 pg/mL), for intact PTH. Close monitoring and individual dose titration are necessary to reach appropriate physiological endpoints. If hypercalcaemia or a persistently elevated corrected Ca x P product greater than 5.2 $mmol^2/L^2$ (65 mg^2/dL^2) is noted, the dose should be reduced or interrupted until these parameters are normalised. Then, paricalcitol administration should be reinitiated at a lower dose. Doses may need to be decreased as the PTH levels decrease in response to therapy.

The following table is a suggested approach for dose titration:

Suggested Dosing Guidelines (Dose adjustments at 2 to 4 week intervals)	
iPTH Level Relative to Baseline	**Paricalcitol Dose Adjustment**
Same or increased Decreased by < 30%	Increase by 2 to 4 micrograms
Decreased by ≥ 30%, ≤ 60%	Maintain
Decreased > 60% iPTH < 15.9 pmol/L (150 pg/mL)	Decrease by 2 to 4 micrograms

PINEWOOD HEALTHCARE
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